REMARKS

In the claims

In claim 34, the terms "sample" or "cells" are amended with the terms "neoplastic" or "neoplastic cells" to provide consistent antecedent basis. These amendments are intended to make the claims more consistent and definite, and are not intended to limit the claims in any way. Further, no new matter is added. Applicants respectfully ask the Examiner to enter the preceding amendments.

Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 34-43 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the enablement requirement. The Examiner states that the claims read on a method of using a mixture of oncolytic viruses for phenotyping, but alleges that the specification does not teach how to use such a mixture. The Examiner alleges that if cancer cells are killed in such a mixture, it is unclear how the phenotype can be determined because it cannot be determined which virus causes the cells' death. The Examiner concludes that the skilled artisan would have to conduct undue and excessive experimentation in order to practice the claimed invention.

The claimed invention is (claim 34):

A method of diagnosing a neoplasm in an animal by phenotype, comprising:

(a) providing a biological sample from the animal, wherein the sample comprises neoplastic cells;

(b) providing at least two oncolytic viruses, wherein each oncolytic virus selectively replicates in neoplastic cells having a phenotype selected from the group consisting of ras pathway activation, interferon-resistance, p53-deficiency and Rb-deficiency; and wherein the at least two oncolytic viruses replicate in neoplastic cells having different phenotypes;

(c) contacting the neoplastic cells in the sample with each of the at least two oncolytic viruses under conditions which allow each oncolytic virus to selectively replicate in the neoplastic cells having the phenotype for which each oncolytic virus is specific;

(d) determining if each of the oncolytic viruses can replicate in the neoplastic cells; and

(e) diagnosing a neoplasm in the animal of a specific phenotype according to the ability of each of the oncolytic viruses to replicate in the neoplastic cells.

The specification teaches that:

> "The present invention provides a method of diagnosing neoplasms having a particular phenotype by using oncolytic viruses that **selectively replicate** in neoplasms having the particular phenotype. For example, reovirus does not replicate in normal cells. However, reovirus **selectively replicate** in cells with an activated ras pathway, which **leads to death of these cells**. ... This invention can further be applied, using other oncolytic viruses" (Abstract, emphasis added)

Thus, a particular virus that "selectively replicates" in cells to the point of leading to "death of these cells" will result in numerous, new copies of that virus. When "at least two oncolytic viruses" are used together, as permitted by the claims, virus that "selectively replicates" will result in more copies of the virus than a virus that does not replicate.

Identification of replicated viruses is readily achieved by standard methods that are well-known to one of ordinary skill in the art. For example, the specification provides:

> The ability of reovirus to infect cells in a sample can be determined by any method in the art. For example, reovirus nucleic acid replication can be measured by polymerase chain reaction with primers specific for the reovirus used; reovirus protein synthesis can be detected by specific antibodies; infected cells can be observed under a microscope and evidence of cytopathic effects induced by the reovirus detected; and replicated reovirus can be harvested from the sample, and virus titer determined, to assess if viral replication has taken place. Other methods of determining the presence of reovirus replication are known to or may be developed by people of ordinary skill in the art. (page 17, paragraph [**0074**])

Also, the specification provides:

> Yet another aspect of the present invention provides a kit comprising a reovirus and a means for detecting replication of the reovirus. The detection means can be a pair of primers specific for the nucleic acid of the reovirus, and may optionally include reagents for PCR. The detection means can also be an antibody specific for a reovirus protein, as well as accompanying reagents such as secondary antibodies. The detection means can further be slides and dyes suitable for observing the morphology of infected cells under the microscope, or virus culture media and cells that can be used to determine the titer of the reovirus. Similarly, the present invention also provides kits comprising another virus capable of replicating in specific tumor cells, as well as means for detecting replication of the virus. Examples of these viruses include, without being limited to, VSV, ONYX-015 virus, and Delta24 virus. (pages 7-8, paragraph [**0037**])

Many of these identification means are or can be selective for a particular virus, for example, polymerase chain reaction with virus-specific primers, specific antibodies for virus proteins, virus-specific culture media and cells, and the like.

Moreover, because such methods can selectively identify viruses, one of ordinary skill in the art can easily distinguish between the "at least two oncolytic viruses" when "determining if each of the oncolytic viruses can replicate in the sample" when the viruses are employed together, e.g., in a mixture, as permitted by the claimed invention. One of ordinary skill in the art can then diagnose "a neoplasm in the animal of a specific phenotype according to the ability of each of the oncolytic viruses to replicate in the sample" as claimed.

Consequently, the specification contains a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to make and use the invention of claims 34-43. The rejection of claims 34-43 under 35 U.S.C. § 112, first paragraph is overcome and Applicants respectfully request that it be withdrawn.

Conclusion

For the reasons set forth above, Applicants submit that the claims of this application are patentable. Reconsideration and withdrawal of the Examiner's objections and rejections are respectfully requested. Allowance of the claims of this application at an early date is earnestly solicited. Please apply any charges or credits to deposit account 06-1050.

Respectfully submitted,

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